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MECHANICAL RESPONSE TISSUE ANALYZER FOR ESTIMATING BONE STRENGTH

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INTRODUCTION

One of the major concerns for extended space flight is weakness of the long bones of the legs, composed primarily of cortical bone, that functions to provide mechanical support. The strength of cortical bone is due to its complex structure, described simplistically as cylinders of parallel osteons composed of layers of mineralized collagen. The reduced mechanical stresses during space flight or immobilization of bone on Earth reduces the mineral content, and changes the components of its matrix and structure so that its strength is reduced (1). Currently, the established clinical measures of bone strength are indirect. They are based on determinations of mineral density by means of radiography, photon absorptiometry, and quantitative computer tomography. While the mineral content of bone is essential to its strength, there is growing awareness of the limitations of the measurement as the sole predictor of fracture risk in metabolic bone diseases, especially osteoporosis (2).

Other experimental methods in clinical trials that more directly evaluate the physical properties of bone, and do not require exposure to radiation, include ultrasound, acoustic emission, and low-frequency mechanical vibration. The last method can be considered a direct measure of the functional capacity of a long bone since it quantifies the mechanical response to a stimulus delivered directly to the bone. A low frequency vibration induces a response (impedance) curve with a minimum at the resonant frequency, that a few investigators use for evaluation of the bone (3). An alternative approach, the method under consideration here, is to use the response curve as the basis for determination of the bone bending stiffness EI and mass, fundamental mechanical properties of bone (4).

DEVELOPMENT OF THE METHOD

Work was initiated by Young and Thompson at Ames Research Center to evaluate the effect of experimental disuse osteoporosis in a non-human primate model for weightlessness (5). The device they developed was an electromagnetic shaker that is placed on the middle of the bone to be tested. They selected the ulna in the arm and the tibia in the leg since both bones have central areas fairly close to the skin surface without a mass of muscle tissue between bone and the probe. A firm clamp held the limb to be tested in a sedated animal, as illustrated in Figure 1. The impedance head is attached to the shaker and the probe placed on the skin is attached to the impedance head so that the stimulus and measurement of the force and acceleration occur at one point.

STUDIES IN THE NON-HUMAN PRIMATE

The force of the vibration causes a deflection from which the average cross-sectional bending stiffness, EI, can be calculated. E is the intrinsic material property and I is the cross-sectional moment of inertia. From this and the length of the bone, the limiting buckling force, Pcr can be computed ($Pcr = EI (\pi/L)^2$). Bending stiffness in Kilo newtons per meter, measured <u>in vivo</u> by this impedance probe technique in the ulna and tibia of the immobilized and recovering monkey are illustrated in Figure 2a. The pattern of decrease in bending stiffness in the left (closed circles) and right (open circles) tibias of 2 adult male monkeys in the absence of weight bearing was consistent, however, the ulna (triangles) in the upper extremity was not. The deficit in strength or bending stiffness present after 6 months required a longer period of time for restoration, i.e., 8 months.

Comparison of the loss of strength in the tibias during disuse seemed to parallel the decreases in bone mineral content, measured by single photon densitometry (Norland) and illustrated in Figure 2b. However, during the 12 month recovery period, there is a clear lag in restoration of mineralization. Although stiffness in the tibias of the animal in the lower panel returned to pre-disuse levels, mineral content remained low for 12 months. This preliminary data emphasizes the importance of direct measures of strength as well as mineral content.

ADVANCES IN THE ANALYSIS SYSTEM

These animal studies coincided with advances in the analysis system to enable a more rapid and efficient measurement. A microprocessor system for analyzing the impedance curves, the "Steele Oxbridge Bone Stiffness Analyzer" was developed to compute the data in seconds instead of hours. The system used a dual channel dynamic signal analyzer (HP3562A) and computer (HP9826A) with dual 3-1/2 inch disk drives and equipment from Bruell and Kjaer for the impedance head (BK4810 - permanent magnet vibration exciter, BK8001 - impedance head, and BK2635 - charge amplifiers). Instead of the standard impedance curve, Steele and his colleagues found it better to work with the ratio of force to displacement obtained from impedance by multiplying by frequency, in the range 0-1600Hz. The result is then expressed in Newtons per meter stiffness or force/displacement.

The resolution of responses from bone was complicated by the need to subtract the resonance from skin and to recognize the damping effect of muscle and resonances from the ends of the bone when they are not firmly positioned. These hurdles were overcome sufficiently to determine the stiffness of the human ulna and verify the theoretical concepts.

BENDING STIFFNESS IN THE HUMAN ULNA

Sufficient data from 4 testing sites have generated results for the ulna that establish the interassay variation between 4% and 5%, an acceptable range for testing on the same day. Both the ability of the test subject to relax and the experience of the operator in positioning the arm influence this considerably. With either a hand held probe or a fixed probe, the variation in the measurement over a month's time averages about 8 percent. It is still uncertain as to whether this variability in subject repeatability is due to actual physiologic changes in the bone or to differences in positioning. Work to automate positioning to reduce this interassay variation from month to month is in progress.

Improved repeatability of the test will be essential for the evaluation of the changes in bone strength that occur in subjects during a ground-based model for weightlessness. Preliminary data in 11 right-handed volunteers for a bed rest study at Ames Research Center indicated biologically valid changes in the stiffness of the ulna. There were decreases in the stiffness of the right ulna in 9 of 11, and increases in stiffness in the left ulna in 8 of 11. These changes were entirely consistent with our current concepts of redistribution of bone mineral in this disuse model and losses in areas of the skeleton where normal function has been disrupted.

The most compelling data for justifying continued efforts to pursue the development of the MRTA has come from the extensive testing of a research instrument in healthy adults and patients at Stanford University and the Palo Alto Veterans Administration Hospital. The relationship of stiffness of the ulna to the bone density of the radius, the adjacent and parallel arm bone, show good correlations (approximately 0.8) that confirm our knowledge of the relationship of strength of bone to the mineral content, we assume to be similar in the radius and ulna. The most important observation for future application of the test has come from a comparison of the axial load capability of the ulna, Pcr, determined from the lateral stiffness measurement, and the bone mineral content of physically active and inactive subjects, as shown in Figure 3. The load capability is higher in the active than inactive subjects for the same value of bone mineral. This data emphasizes the importance of the quality of bone for its functional capability, as well as its mineral content.

CLINICAL INSTRUMENTATION

The most recent advances in the development of the MRTA have been in the design and construction of a clinically useful instrument carried out by Gaitscan, Inc. Automatic centering of the probe on the long bone to be tested and an adjustable limb support that can be easily raised, lowered or moved horizontally to accommodate the variety in body types, has greatly reduced the time of the test and increased subject acceptance. The design of the limb support has enabled us to acquire data in the tibia, the bone in the leg that is most vulnerable to space flight. The more irregular shape of the tibia than the ulna or other factors make it a more difficult bone to measure with reliability. Nevertheless, our preliminary data shows a good correlation of stiffness with bone mineral content and stiffness values in the range theoretically estimated for a beam of larger dimensions and mass than the ulna. Refinements of instrument design and of the data analysis to reduce the variation in the test results, higher in the tibia than in the ulna, are in progress. With this newly constructed instrument it is possible to test large numbers of people.

APPLICATIONS OF BONE STIFFNESS TESTING

The application of a non-invasive direct measurement of the strength of long bones is most obviously to the identification of individuals with deficits due to a variety of causes, and to the monitoring of treatment programs aimed at correcting the deficits. While there has been considerable interest in the diagnosis and prediction of fracture in patients with senile or post-menopausal osteoporosis, one of the major national health problems, there is now no firm data that indicates the value of this measure of bone strength to be superior to the newer radiographic methods for diagnosis. Bone diseases in which trabecular bone is the primary target would require extensive clinical testing in patients with evidence of cortical bone involvement to evaluate the utility of the MRTA. The more immediate applications of the MRTA in medicine are in the follow-up of osteoporotic patients or others receiving various treatments directed at improving deficits in mineral and/or strength as well as patient activity. The effects of fitness programs carried out for any purpose at any age and patient population can be easily monitored with the MRTA.

Aside from the importance of a direct measure of a physical property of bone to the astronaut, the safety and simplicity of the bone strength test lends itself to screening studies aimed at identifying substandard individuals, with respect to bone quality. Surveys of military recruits, high school and college age students would be particularly informative for those interested in the musculoskeletal fitness status of the nation.

REFERENCES

1. Patterson-Buckendahl, P., Arnaud, S. B., Mechanic, G. L., Martin, R. B., Grindeland, R. E., and Cann, C. E. Fragility and composition of growing rat bone after one week in spaceflight. Am. J. Physiol. 252 (Regulatory Integrative Comp. Physiol. 21): R240-R246, 1987.

2. Ott, S. M., Kilcoyne, R. F., and Chestnut, C. H. III. Comparisons among methods of measuring bone mass and relationship to severity of vertebral fractures in osteoporosis. J. Clin. Endocrinol. Metab. 66: 501-507, 1988.

3. Doherty, W. P., Bovill, E. G., and Wilson, E. L. Evaluation of the use of resonant frequencies to characterize physical properties of human long bones. J. Biomechanics 7: 559-561, 1974.

4. Steele, C. R., Zhou, L.-J., Guido, D., Marcus, R., Heinrichs, W. L., and Cheema, C. Noninvasive determination of ulnar stiffness from mechanical response -- <u>in vivo</u> comparison of stiffness and bone mineral content in humans. ASME J. Biomech. Eng. 110: 87-96, 1988.

5. Thompson, G. A., Orne, D., and Young, D. R. In vivo determination of mechanical properties of the human ulna by means of mechanical impedance tests: Experimental results and improved mathematical model. Med. Biol. Eng. 14: 253-262, 1976.

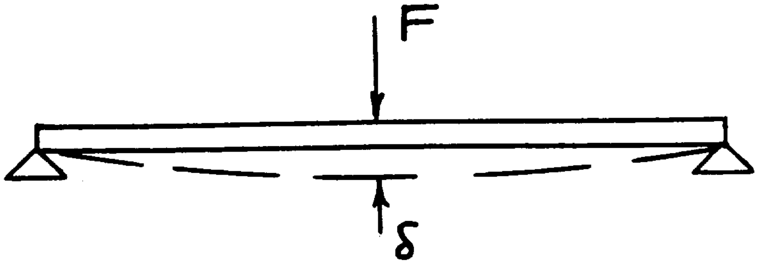
6. Young, D. R., Howard, W. H., Cann, C., and Steele, C. R. Noninvasive measures of bone bending in the monkey (M. nemestrina). Calcif. Tissue 27: 109-115, 1979.

7. Young, D. R., Niklowitz, W. J., and Steele, C. R. Tibial changes in experimental disuse osteoporosis in the monkey. Calcif. Tissue Int. 35: 304-308, 1983.

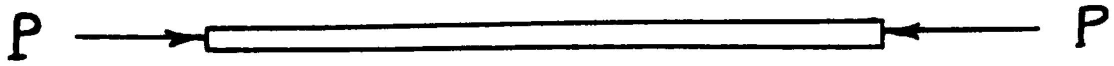
8. Steele, C. R. and Gordon, A. F. Preliminary clinical results for "SOBSA" noninvasive measurement of ulnar bending stiffness. ASME Advances in Bioengineering, R. C. Eberhard and A. H. Burstein, eds., pp 85-87.

9. Arnaud, S. B. and Morey-Holton, E. Gravity, Calcium and Bone: Update, 1989. The Physiologist 33: S65-S68, 1990.

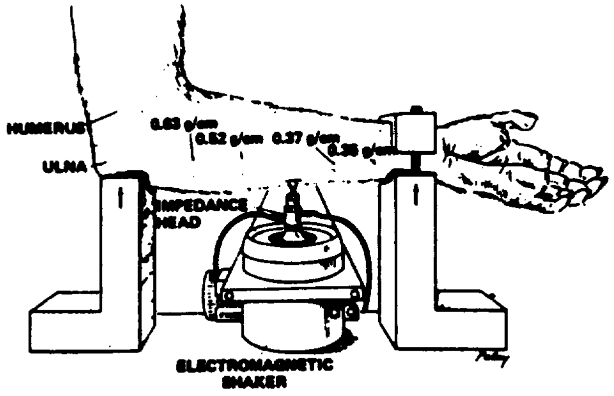
FIGURE 1. From Steele, C. R., Proc. Workshop on Advances in NASA-Relevant Minimally Invasive Instrumentation, 1984. JPL D-1942.



A beam, supported on the ends, when loaded by the force F will deflect the distance δ. The lateral stiffness is $k = f/\delta$.



A beam with compression force P. The limiting force is the buckling load P_{cr}, which can be computed from the lateral stiffness.



Noninvasive measurement of ulnar stiffness in monkey.
(from reference 6)

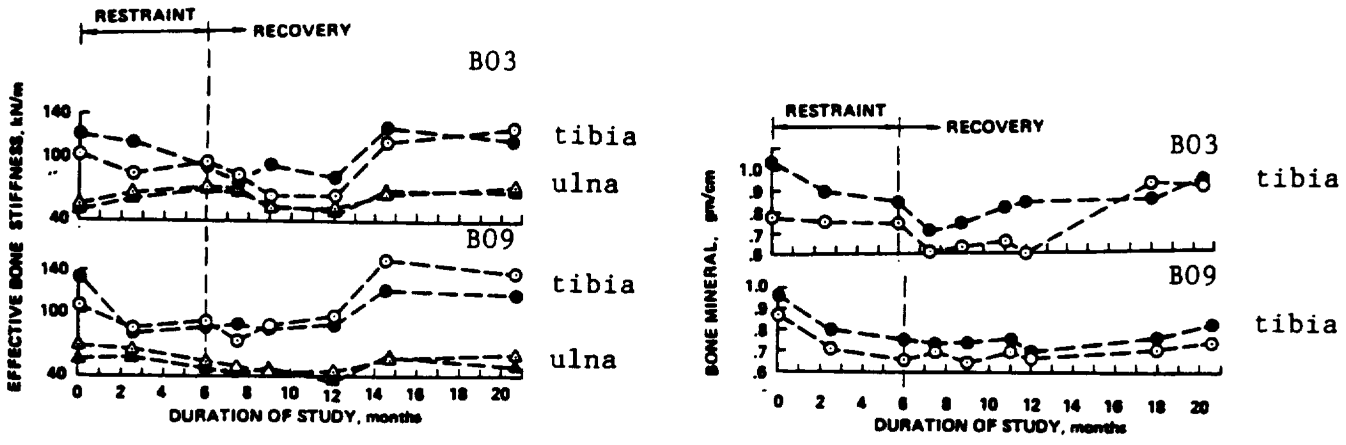
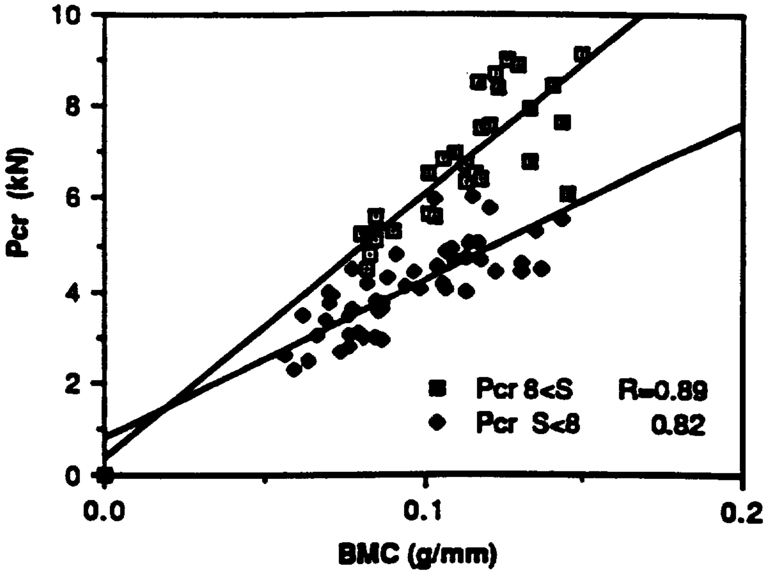


FIGURE 2. Adapted from reference 6



Comparison of axial load capability of ulna Pcr, determined from lateral stiffness measurement, and bone mineral content.

FIGURE 3. From reference 6